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|---|-------------|----------------------|---------------------|------------------|
| 10/575,033  | 01/08/2008  | Wei-Chiang Shen      | 89188.0151          | 5935             |
| 26/021 7590 08/19/2010<br>Hogan Lovells US LLP<br>1999 AVENUE OF THE STARS<br>SUITE 1400<br>LOS ANGELES, CA 90067 |             |                      |                     |                  |
| EXAMINER<br>CHANDRA, GYAN   |             |                      |                     |                  |
| ART UNIT  |             | PAPER NUMBER         |                     |                  |
| 1646  |             |                      |                     |                  |
| NOTIFICATION DATE   |             | DELIVERY MODE        |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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### Office Action Summary

**Application No.**

10/575,033

**Applicant(s)**

SHEN ET AL.

**Examiner**

GYAN CHANDRA

**Art Unit**

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 June 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1.5 and 8-30 is/are pending in the application.
- 4a) Of the above claim(s) 12-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1.5 and 8-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's response filed on 6/10/2010 is acknowledged and fully considered.

#### ***Status of Application, Amendments, And/Or Claims***

The amendments of claims 1, 5 and 8-11, and the cancellation of claims 2-4, and 6-7 have been made of record.

Claims 1, 5 and 8-30 are pending. Claims 12-30 remain withdrawn for the reasons of record on pg. 2 of the Office Action of 12/11/2009.

Claims 1, 5, and 8-11 are under examination.

#### ***Claim Objections***

Claim 9 is objected because it recites "wherein the order of the G-CSF domain and the Tf domain is from the N-terminus to the C-terminus" It is noted that all the proteins run from N-terminus to C-terminus. If Applicant meant to be that the G-CSF domain is N-terminus to the Tf, then the claim should be amended to "wherein the G-CSF domain is N-terminus to the Tf domain"

#### ***Response to Arguments***

##### ***Claim Rejections - 35 USC § 112-withdrawn***

The rejection of claims 10 and 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicants' amendments to the claims.

***Claim Rejections - 35 USC § 103-withdrawn***

The rejection of claims 1, 3, and 5-7 under 35 U.S.C. 103(a) as being unpatentable over Widera et al in view of Friden et al ( US Patent No. 5,672,683) is withdrawn in view of Applicants' cancellation of claims 3, 6 and 7.

**Brief Description of the Figures**

The Brief Description of the Figures remains objected because Figure 8 comprises part (a) and (b) to be labeled as Figure 8 (a)-(b) for the reasons of record on pg. 2 of the Office Action of 12/11/2009. Applicants argue that only they need to describe what Figure 8 (a) and (b) are in the Brief Description. This has been considered but not persuasive because the Brief Description should describe exactly what the figure legend says.

***Claim Rejections - 35 USC § 102-maintained***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 5 and 9-11 remain rejected under 35 U.S.C. 102(a) as being anticipated by Widera et al (previously presented, Pharmaceutical Res. 20: 1231-1238, 2003 for the reasons of record on pg. 3-5 of the Office Action of 12/11/09 and as discussed below.

The instant claims are broadly drawn to a fusion polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferring (Tf) domain, wherein the ability of the polypeptide to be transported into a cell expressing a transferring receptor (TfR) gene or the ability of the polypeptide to be transported across a cell expressing a TfR gene via transcytosis is higher than that of the G-CSF domain alone (claim 1), wherein the polypeptide is a recombinant polypeptide (claim 5), wherein the order of the G-CSF domain and the Tf domain is from the N-terminus to the C-terminus (Claim 9), wherein Tf domain may bind one iron molecules (claims 10), and wherein Tf domain may bind two iron molecules (claims 11).

Applicants argue that the reference Widera cannot anticipate or render claim 1 obvious because the reference does not teach or suggest a fusion polypeptide comprising G-CSF and Tf. They argue that Widera does not teach any possible advantages a fusion protein may have over a conjugate. They argue that the specification on pg. 23 teaches advantages of a fusion protein over a conjugate.

Applicants' arguments have been fully considered but they are not persuasive because the instantly claimed invention is drawn to a fusion polypeptide comprising a granulocyte colony stimulating factor domain operatively linked to a transferring domain. The specification on page 1 lines 13+ discloses that the present invention relates to G-CSF-transferrin fusion protein (e.g., conjugate and recombinant proteins). The specification on page 9 defines "G-CSF-Tf fusion protein" as a composite protein containing both a G-CSF domain and a Tf domain. The reference Widera et al teaches a polypeptide conjugate comprising G-CSF and transferrin linked with a disulfide bond

(page 1232, preparation of Tf-GCSF conjugate). In response to Applicants' arguments that the reference does not teach advantages of a fusion protein produced by recombinant technology, it is well known in the art that a recombinant protein can be produced and purified in large quantity at a lower price. Therefore, the fusion polypeptide includes a conjugate polypeptide (as supported by the instant specification, pg. 9). Therefore, the prior art of record anticipates the instantly claimed invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,5 and 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Widera et al in view of Prior et al (US Patent No. 7,176,278) for the reasons of record on pg. 5-9 of the Office Action of 12/11/2009 and as discussed below.

The instant claims are broadly drawn to a fusion polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferring (Tf) domain, wherein the fusion polypeptide is a recombinant polypeptide, and wherein the fusion polypeptide further comprises a secretion signal at the N-terminus.

Applicants argue that the reference Widera et al does not teach a fusion polypeptide and therefore, the reference Prior does not remedy the defect of Widera et al. They argue that the reference Prior teaches making expression construct comprising a transcriptional promoter, a secretory signal sequence, and a nucleic acid sequence encoding a modified Tf fusion protein but this does not teach encoding a fusion polypeptide comprising a G-CSF and Tf domain.

Applicants' arguments have been fully considered but they are not persuasive because the reference Widera et al teaches conjugate between a G-CSF and Tf which meets the limitation of a fusion protein as described in the specification (see pg. 9). Additionally, the reference Prior et al teaches a fusion protein between Tf and another protein (e.g., EMP1/Tf (Example 2), GLP-1/Tf (Example 3), beta IFF/Tf (Example 4),

and soluble Toxin receptor/Tf (Example 5)). Therefore, it would have obvious to one of the skill in the art to make the instantly claimed invention.

***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **GYAN CHANDRA** whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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